CLAIMS

[1] A humanized antibody binding to CD47.

[2] The humanized antibody of claim 1 wherein CD47 is human CD47.

[3] The humanized antibody of claim 1 or 2 wherein the CDRs of the humanized antibody are derived from a mouse antibody.

[4] The humanized antibody of any one of claims 1 to 3 comprising any one of the sequence sets below:

(1) the sequence of aa 31-35 (CDR1), the sequence of aa 50-66 (CDR2), and the sequence of aa 99-106 (CDR3) of SEQ ID NO: 7;

(2) the sequence of aa 31-35 (CDR1), the sequence of aa 50-66 (CDR2), and the sequence of aa 99-106 (CDR3) of SEQ ID NO: 10;

(3) the sequence of aa 31-35 (CDR1), the sequence of aa 50-66 (CDR2), and the sequence of aa 99-106 (CDR3) of SEQ ID NO: 13;

(4) the sequence of aa 31-35 (CDR1), the sequence of aa 50-66 (CDR2), and the sequence of aa 99-106 (CDR3) of SEQ ID NO: 16;

(5) the sequence of aa 31-35 (CDR1), the sequence of aa 50-66 (CDR2), and the sequence of aa 99-106 (CDR3) of SEQ ID NO: 19

(6) the sequence of aa 31-35 (CDR1), the sequence of aa 50-66 (CDR2), and the sequence of aa 99-106 (CDR3) of SEQ ID NO: 22;

(7) the sequence of aa 31-35 (CDR1), the sequence of aa 50-66 (CDR2), and the sequence of aa 99-106 (CDR3) of SEQ ID NO: 30;

(8) the sequence of aa 24-39 (CDR1), the sequence of aa 55-61 (CDR2), and the sequence of aa 94-102 (CDR3) of SEQ ID NO: 37;

(9) the sequence of aa 24-39 (CDR1), the sequence of aa 55-61 (CDR2), and the sequence of aa 94-102 (CDR3) of SEQ ID NO: 40;

(10)the sequence of aa 24-39 (CDR1), the sequence of aa 55-61 (CDR2), and the sequence of aa 94-102 (CDR3) of SEQ ID NO: 43;

(11) the sequence of aa 24-39 (CDR1), the sequence of aa 55-61 (CDR2), and the sequence of aa 94-102 (CDR3) of SEQ ID NO: 46;

(12) the sequence of aa 24-39 (CDR1), the sequence of aa 55-61 (CDR2), and the sequence of aa 94-102 (CDR3) of SEQ ID NO: 49;

(13) the sequence of aa 24-39 (CDR1), the sequence of aa 55-61 (CDR2), and the sequence of aa 94-102 (CDR3) of SEQ ID NO: 52;

(14) the sequence of aa 24-39 (CDR1), the sequence of aa 55-61 (CDR2), and the sequence of aa 94-102 (CDR3) of SEQ ID NO: 57;

(15) the sequence of aa 31-35 (CDR1), the sequence of aa 50-66 (CDR2), and the sequence of aa 99-106 (CDR3) of SEQ ID NO: 64; and

(16) the sequence of aa 24-39 (CDR1), the sequence of

aa 55-61 (CDR2), and the sequence of aa 94-102 (CDR3) of SEQ ID NO: 67.

[5] The humanized antibody of any one of claims 1 to 3 comprising any one of the sequence sets below:

(1) the sequence of aa 1-30 (FR1), the sequence of aa 36-49 (FR2), the sequence of aa 67-98 (FR3), and the sequence of aa 107-117 (FR4) of SEQ ID NO: 7;

(2) the sequence of aa 1-30 (FR1), the sequence of aa 36-49 (FR2), the sequence of aa 67-98 (FR3), and the sequence of aa 107-117 (FR4) of SEQ ID NO: 10;

(3) the sequence of aa 1-30 (FR1), the sequence of aa 36-49 (FR2), the sequence of aa 67-98 (FR3), and the sequence of aa 107-117 (FR4) of SEQ ID NO: 13;

(4) the sequence of aa 1-30 (FR1), the sequence of aa 36-49 (FR2), the sequence of aa 67-98 (FR3), and the sequence of aa 107-117 (FR4) of SEQ ID NO: 16;

(5) the sequence of aa 1-30 (FR1), the sequence of aa 36-49 (FR2), the sequence of aa 67-98 (FR3), and the sequence of aa 107-117 (FR4) of SEQ ID NO: 19;

(6) the sequence of aa 1-30 (FR1), the sequence of aa 36-49 (FR2), the sequence of aa 67-98 (FR3), and the sequence of aa 107-117 (FR4) of SEQ ID NO: 22;

(7) the sequence of aa 1-30 (FR1), the sequence of aa 36-49 (FR2), the sequence of aa 67-98 (FR3), and the sequence of aa 107-117 (FR4) of SEQ ID NO: 30;

(8) the sequence of aa 1-23 (FR1), the sequence of aa 40-54 (FR2), the sequence of aa 62-93 (FR3), and the sequence of aa 103-112 (FR4) of SEQ ID NO: 37;

(9) the sequence of aa 1-23 (FR1), the sequence of aa 40-54 (FR2), the sequence of aa 62-93 (FR3), and the sequence of aa 103-112 (FR4)of SEQ ID NO: 40;

(10) the sequence of aa 1-23 (FR1), the sequence of aa 40-54 (FR2), the sequence of aa 62-93 (FR3), and the sequence of aa 103-112 (FR4) of SEQ ID NO: 43;

(11) the sequence of aa 1-23 (FR1), the sequence of aa 40-54 (FR2), the sequence of aa 62-93 (FR3), and the sequence of aa 103-112 (FR4) of SEQ ID NO: 46;

(12) the sequence of aa 1-23 (FR1), the sequence of aa 40-54 (FR2), the sequence of aa 62-93 (FR3), and the sequence of aa 103-112 (FR4) of SEQ ID NO: 49;

(13) the sequence of aa 1-23 (FR1), the sequence of aa 40-54 (FR2), the sequence of aa 62-93 (FR3), and the sequence of aa 103-112 (FR4) of SEQ ID NO: 52;

(14) the sequence of aa 1-23 (FR1), the sequence of aa 40-54 (FR2), the sequence of aa 62-93 (FR3), and the sequence of aa 103-112 (FR4) of SEQ ID NO: 57;

(15) the sequence of aa 1-30 (FR1), the sequence of aa 36-49 (FR2), the sequence of aa 67-98 (FR3), and the sequence of aa 107-117 (FR4) of SEQ ID NO: 64; and

(16) the sequence of aa 1-23 (FR1), the sequence of aa 40-54 (FR2), the sequence of aa 62-93 (FR3), and the sequence of aa 103-112 (FR4) of SEQ ID NO: 67.

[6] The humanized antibody of any one of claims 1 to 5, which is a small antibody fragment.

[7] The humanized antibody of claim 6, which is a diabody.

[8] The humanized antibody of claim 7, which is a single-chain diabody.

[9] The humanized antibody of claim 7 or 8, characterized in that a disulfide bond exists between diabody-forming fragments.

[10] The humanized antibody of claim 9 characterized by:

(1) an antibody having the amino acid sequence of SEQ ID NO: 90; or

(2) an antibody having an amino acid sequence containing a deletion, addition or substitution of one or several amino acid(s) in the amino acid sequence of (1) and having CD47-binding activity.

[11] The humanized antibody of claim 9 characterized by:

(1) an antibody having the amino acid sequence of SEQ ID NO: 92; or

(2) an antibody having an amino acid sequence containing a deletion, addition or substitution of one or several amino acid(s) in the amino acid sequence of (1) and having CD47-binding activity.

[12] A diabody antibody binding to human CD47, characterized in that a disulfide bond exists between diabody-forming fragments.

[13] The diabody antibody of claim 12 comprising any one of the sequence sets below:

(1) the sequence of aa 31-35 (CDR1), the sequence of aa 50-66 (CDR2), and the sequence of aa 99-106 (CDR3) of SEQ ID NO: 7;

(2) the sequence of aa 31-35 (CDR1), the sequence of

aa 50-66 (CDR2), and the sequence of aa 99-106 (CDR3) of SEQ ID NO: 10;

(3) the sequence of aa 31-35 (CDR1), the sequence of aa 50-66 (CDR2), and the sequence of aa 99-106 (CDR3) of SEQ ID NO: 13;

(4) the sequence of aa 31-35 (CDR1), the sequence of aa 50-66 (CDR2), and the sequence of aa 99-106 (CDR3) of SEQ ID NO: 16;

(5) the sequence of aa 31-35 (CDR1), the sequence of aa 50-66 (CDR2), and the sequence of aa 99-106 (CDR3) of SEQ ID NO: 19

(6) the sequence of aa 31-35 (CDR1), the sequence of aa 50-66 (CDR2), and the sequence of aa 99-106 (CDR3) of SEQ ID NO: 22;

(7) the sequence of aa 31-35 (CDR1), the sequence of aa 50-66 (CDR2), and the sequence of aa 99-106 (CDR3) of SEQ ID NO: 30;

(8) the sequence of aa 24-39 (CDR1), the sequence of aa 55-61 (CDR2), and the sequence of aa 94-102 (CDR3) of SEQ ID NO: 37;

(9) the sequence of aa 24-39 (CDR1), the sequence of aa 55-61 (CDR2), and the sequence of aa 94-102 (CDR3) of SEQ ID NO: 40;

(10)the sequence of aa 24-39 (CDR1), the sequence of aa 55-61 (CDR2), and the sequence of aa 94-102 (CDR3) of SEQ ID NO: 43;

(11) the sequence of aa 24-39 (CDR1), the sequence of aa 55-61 (CDR2), and the sequence of aa 94-102 (CDR3) of

SEQ ID NO: 46;

(12) the sequence of aa 24-39 (CDR1), the sequence of aa 55-61 (CDR2), and the sequence of aa 94-102 (CDR3) of SEQ ID NO: 49;

(13) the sequence of aa 24-39 (CDR1), the sequence of aa 55-61 (CDR2), and the sequence of aa 94-102 (CDR3) of SEQ ID NO: 52;

(14) the sequence of aa 24-39 (CDR1), the sequence of aa 55-61 (CDR2), and the sequence of aa 94-102 (CDR3) of SEQ ID NO: 57;

(15) the sequence of aa 31-35 (CDR1), the sequence of aa 50-66 (CDR2), and the sequence of aa 99-106 (CDR3) of SEQ ID NO: 64; and

(16) the sequence of aa 24-39 (CDR1), the sequence of aa 55-61 (CDR2), and the sequence of aa 94-102 (CDR3) of SEQ ID NO: 67.

[14] A humanized antibody binding to CD47 comprising:

(1) a heavy chain variable region containing the sequence of aa 1-117 of SEQ ID NO: 30: and

(2) a light chain variable region containing the sequence of aa 1-112 of SEQ ID NO: 57.

[15] A humanized antibody binding to CD47 comprising:

(1) a heavy chain variable region containing the sequence of aa 1-117 of SEQ ID NO: 64: and

(2) a light chain variable region containing the sequence of aa 1-112 of SEQ ID NO: 67.

[16] An antibody binding to CD47 comprising any one of:

(1) the sequence of aa 1-234 of SEQ ID NO: 73;

(2) the sequence of aa 1-234 of SEQ ID NO: 74;

(3) the sequence of aa 1-483 of SEQ ID NO: 78; and

(4) the sequence of aa 1-483 of SEQ ID NO: 79.

[17] A gene encoding the antibody of any one of claims 1 to 16.

[18] A vector containing the gene of claim 17.

[19] A host cell containing the vector of claim 18.

[20] A process for preparing an antibody, comprising the step of culturing the host cell of claim 19.

[21] A therapeutic agent for hematological disorder, comprising the antibody of any one of claims 1 to 16.

[22] The therapeutic agent of claim 21 wherein the hematological disorder is selected from leukemias such as acute myelocytic leukemia, chronic myelocytic leukemia, acute lymphocytic leukemia, chronic lymphocytic leukemia, adult T-cell leukemia, multiple myeloma, mixed leukemia, and hairy cell leukemia; malignant lymphoma (Hodgkin's disease, non-Hodgkin's lymphoma), aplastic anemia, myelodysplastic syndromes, and polycythemia vera.